You Ready For It? Insights Into Progressive Diabetes Management

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OHIO PHARMACISTS ASSOCIATION

1 VOICE VISION TEAM

Disclosure Statement

- Sarah Aldrich Renner + Marilee Clemons have no relevant financial relationship(s) with ineligible companies to disclose.

  and

- None of the planners for this activity have relevant financial relationships with ineligible companies to disclose.

Learning Objectives

At the completion of this activity, the participant will be able to:

1. Discuss diabetes management updates for pharmacists
2. Summarize pharmacotherapeutic and nonpharmacotherapeutic approaches for management of diabetes
3. Select an appropriate patient specific treatment and monitoring plan for diabetes

Language

Important to incorporate person-first and inclusive language that empowers patients and recognizes that patients are at the center of diabetes care

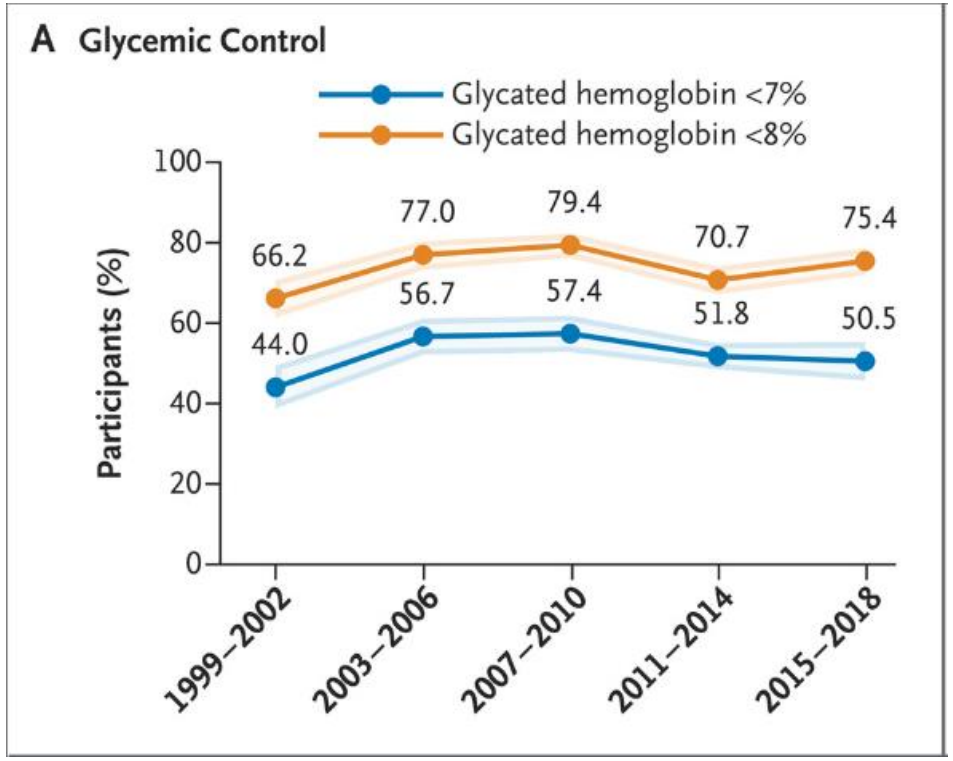
AVOID	RECOMMEND
Diabetic	Person with diabetes
Test	Monitor
Control	Manage
Unrealistic goals	High expectations for self-management
Suffering from diabetes	Living with diabetes
Good/bad/poor glycemic control	Hemoglobin A1C (HbA1C), HbA1C levels, glycemic targets
Compliance or adherence	Engagement, medication-taking
Obese, morbidly obese, fat	Excess body weight, weight, body mass index (BMI)

DiaTribe Learn. "Diabetes Language Recommendations: How to Avoid Judgement and Stigma".https://diatribe.org/diabetes-language-recommendations-how-avoid-judgment-and-stigma

BACKGROUND

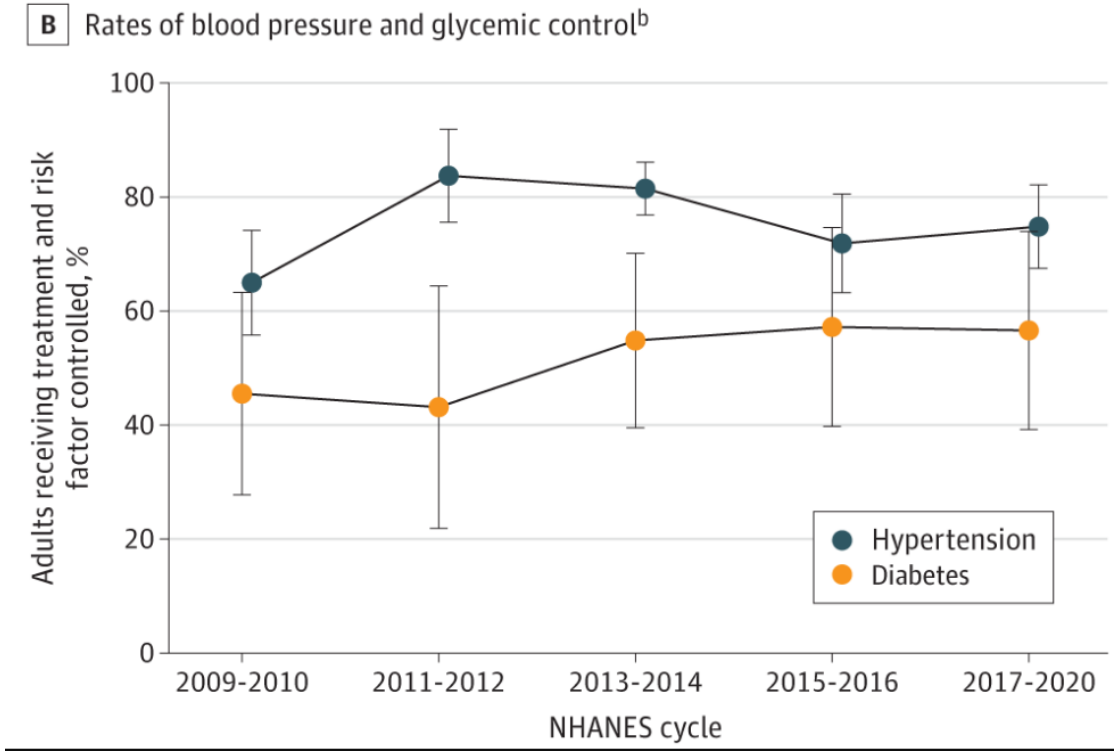
Stagnation of Diabetes Management

All Adults



Fang M, et al. NEJM.2021;384:2219-2228

Adults Age 20-44 Years



Aggarwal R, et al. JAMA.2023;329(11):899-909

Barriers to Glycemic Control

Patients

- Medication access
- Social Determinants of Health (SDOH)
- Limited understanding of diabetes (DM)
- Diabetes Self-Management Education and Support Services (DSMES) and Medical Nutrition Therapy (MNT) access
- Complexity of disease state/regimen
- Communication/trust
- Lack of support

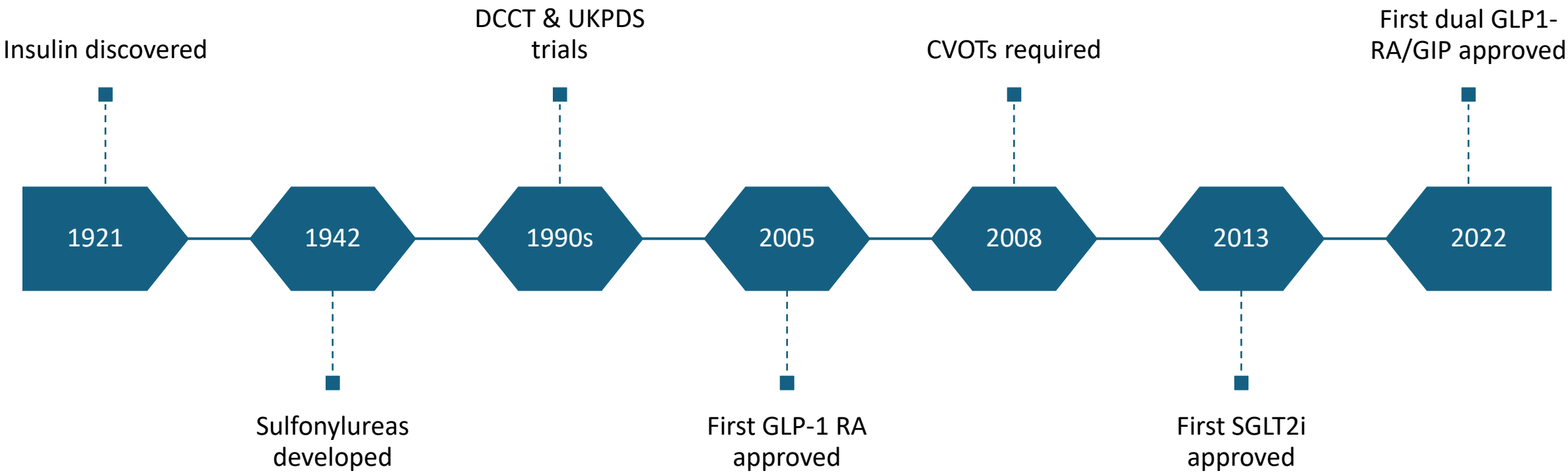
Providers

- Time constraints
- Lack of goals for therapy
- Side effect concerns
- Low referrals to DSMES, MNT, and other non-pharm options

Systems/Payers

- Lack of population health initiatives
- Lack of team-based approach
- Lack of formulary transparency
- Lack of coverage for needed services

The Last 100 Years..

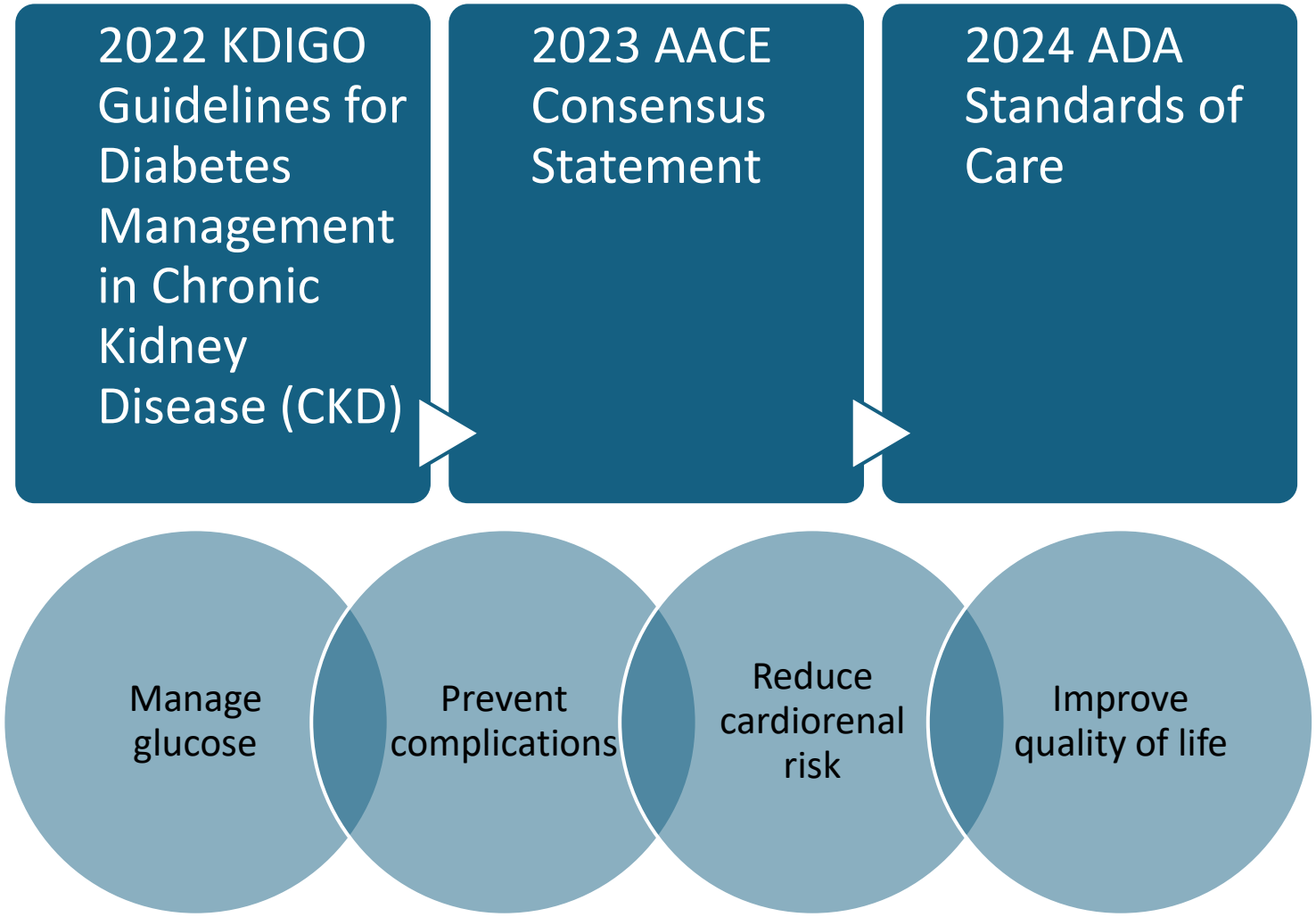


DCCT: Diabetes Control and Complications Trial
UKPDS: UK Prospective Diabetes Study
CVOT: Cardiovascular outcome trial

GLP1-RA: Glucagon-like peptide-1 receptor agonist
SGLT2i: Sodium glucose co-transporter 2 inhibitor
GLP1-RA/GIP: Glucagon-like peptide-1 receptor agonist/glucose-dependent insulinotropic polypeptide

Frias J et al. NEJM 2021;385:503-515

Guideline Shift?



KDIGO: Kidney Disease | Improving Global Outcomes
AACE: American Association of Clinical Endocrinology
ADA: American Diabetes Association

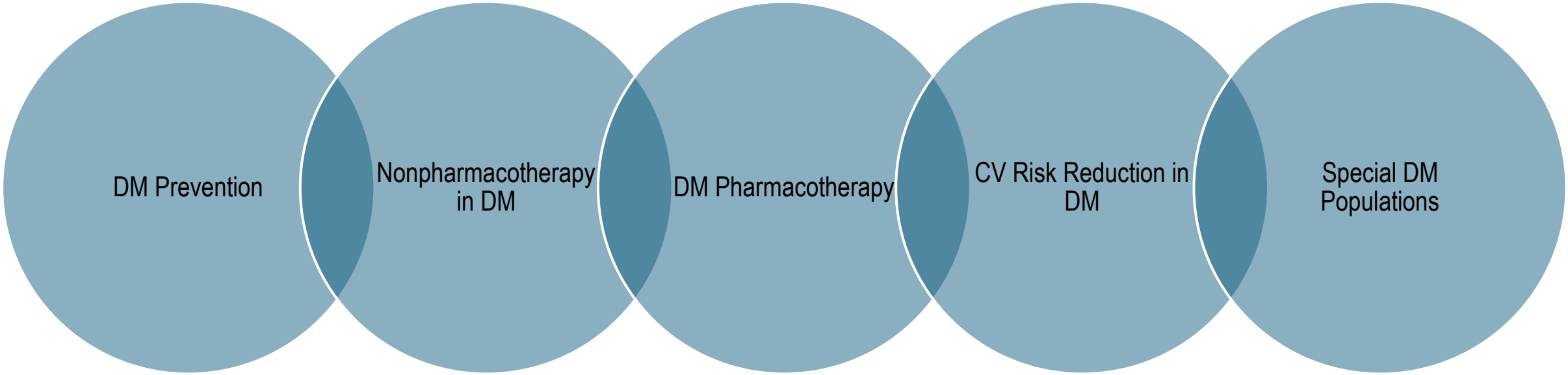
DM Targets

Most Patients with Diabetes	
HbA1C	< 7.0% (ADA) or < 6.5% (AACE)
Blood Glucose Monitor (BGM) Users	
Fasting blood glucose (BG)	80 – 130 mg/dL (ADA) or 70 – 110 mg/dL (AACE)
2 hour post prandial BG	< 180 mg/dL (ADA) or < 140 mg/dL (AACE)
Continuous Glucose Monitor (CGM) Users	
Time in range (70 – 180)	> 70%
Time below range (<70)	< 4%

*Less stringent targets for: patients with history of severe hypoglycemia, limited life expectancy, advanced MICRO/MACRO complications, extensive co-morbidities, long-standing DM, etc.

AACE. Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm. 2023

Topic Map


DM Prevention
Nonpharmacotherapy in DM
DM Pharmacotherapy
CV Risk Reduction in DM
Special DM Populations

DIABETES PREVENTION

Prevention or Delay of Diabetes

Lifestyle + Behavior Change

- Weight loss, diet changes, physical activity

Diabetes Prevention Program

Pharmacologic Interventions

- Metformin
- Weight loss medications (orlistat, phentermine/topiramate, liraglutide, semaglutide and tirzepatide)

Prevention of Vascular Disease + Mortality

- Screen and treat modifiable cardiovascular (CV) risk factors
- Statins may increase risk of Type 2 Diabetes Mellitus (T2DM) in pre-DM, do not discontinue if taking
- Pioglitazone (pre-DM and stroke hx)

Person-Centered Care Goals

ADA. Standards of Care. 2024.

Obesity and Weight Management

Weight loss of 3-7%: improves glycemia, reduces other immediate CV risk factors

Weight loss of >10%: potential disease modifying effects (including remission of T2DM) and may improve long term CV risk

Nutrition, Physical Activity and Behavioral Therapy	Pharmacotherapy	Metabolic Surgery
• Use to achieve and maintain ≥ 5% weight loss • High frequency counseling interventions or structured programs • Individualized treatment important to achieve weight loss	• Minimize medications associate with weight gain • Consider pharmacotherapy in addition to lifestyle changes • GLP1-RA or GIP/GLP1-RA preferred in patients with T2DM	• Consider in T2DM with BMI ≥ 30 kg/m2 • Long-term medical support, behavioral support and metabolic monitoring required post-surgery

ADA. Standards of Care. 2024.

Obesity Pharmacotherapy

Short-Term Therapy				
Medication + Doses	**Class**	**Weight Loss (% from baseline)**	**Common Side Effects**	**Cost**
Phentermine 8-37.5 mg daily	Sympathomimetic amine anorectic	4.9-5.0% (placebo 1.9%)	Dry mouth, insomnia, irritability, increased blood pressure (BP), elevated heart rate (HR)	$
Long-Term Therapy				
Medication(s) + Doses	**Class**	**Weight Loss (% from baseline)**	**Common Side Effects**	**Cost**
Orlistat 60-120 mg TID	Lipase inhibitor	9.6% (placebo 5.6%)	Abdominal pain, flatulence, fecal urgency	$$
Naltrexone/bupropion ER 16mg/180 mg BID	Opioid antagonist/antidepressant combination	5.0% (placebo 1.8%)	Constipation, nausea, headache, xerostomia, increased BP, elevated HR	$$
Phentermine/topiramate ER 7.5mg/46mg daily	Sympathomimetic amine anorectic/antiepileptic combination	7.8-9.7% (placebo 1.2%)	Constipation, paresthesia, insomnia, nasopharyngitis, xerostomia, increased BP	$$
Liraglutide 3 mg daily Semaglutide 2.4 mg weekly	GLP-1 RA	4.7-6.0% (placebo 2%) 7-9.6% (placebo 3.4%)	Gastrointestinal (GI), injection site reaction, elevated HR, hypoglycemia	$$$
Tirzepatide 5mg, 10mg, or 15 mg weekly	GIP/GLP-1RA	12.8-14.7% (placebo 3.2%)	GI, injection site reaction, elevated HR, hypoglycemia	$$$

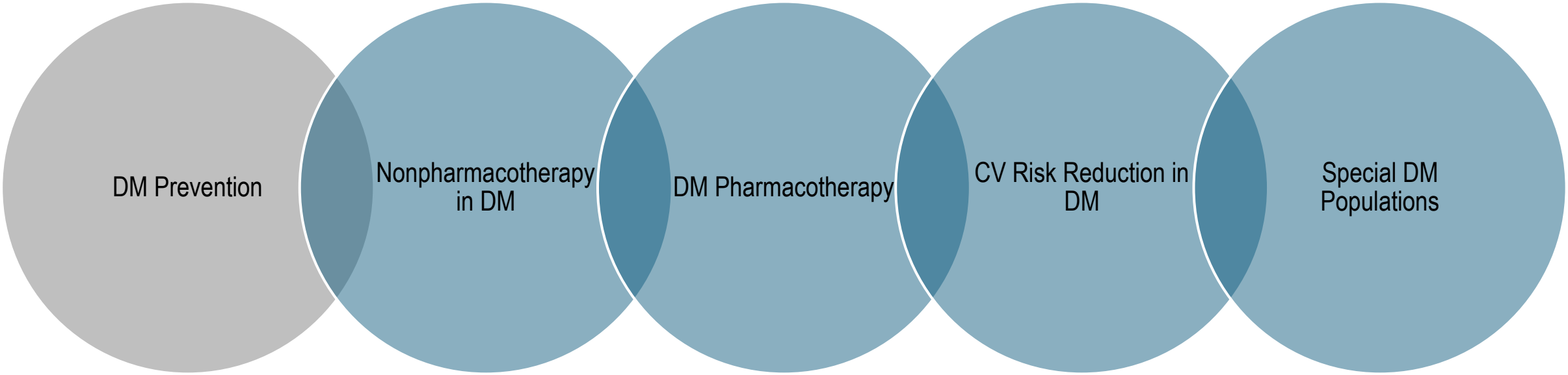
ADA. Standards of Care. 2024. Adapted from table 8.1

SELECT – Semaglutide + CV Outcomes in Obesity without DM

Population	17604 patients with cardiovascular disease (CVD) and BMI ≥ 27 kg/m2 without diabetes followed for a mean of 39.8 months
Methods	•Semaglutide 2.4 mg weekly or placebo •Primary outcome: composite of death from CV causes, nonfatal MI or nonfatal stroke
Results	•Primary endpoint occurred in 6.5% of semaglutide patients vs 8.0% of placebo patients (P<0.001) •More adverse events in the semaglutide group, 16.6% vs 8.2% in placebo (P<0.001)
Takeaway	•Semaglutide reduced incidence of death from CV causes, nonfatal MI or nonfatal stroke compared to placebo in patients with CVD and obesity

Lincoff AM, et al. N Engl J Med. 2023.

Topic Map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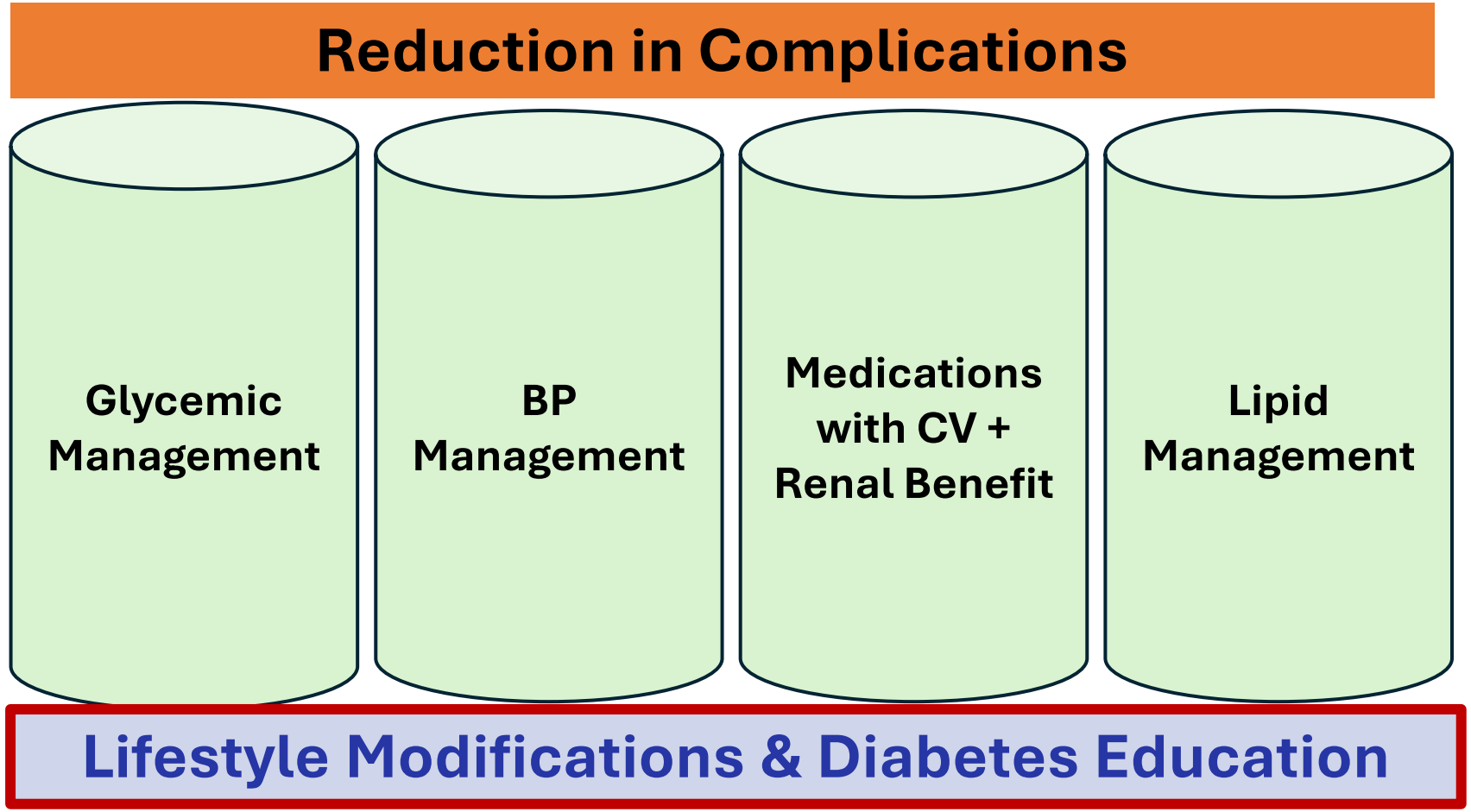
DIABETES TREATMENT

nonpharmacologic

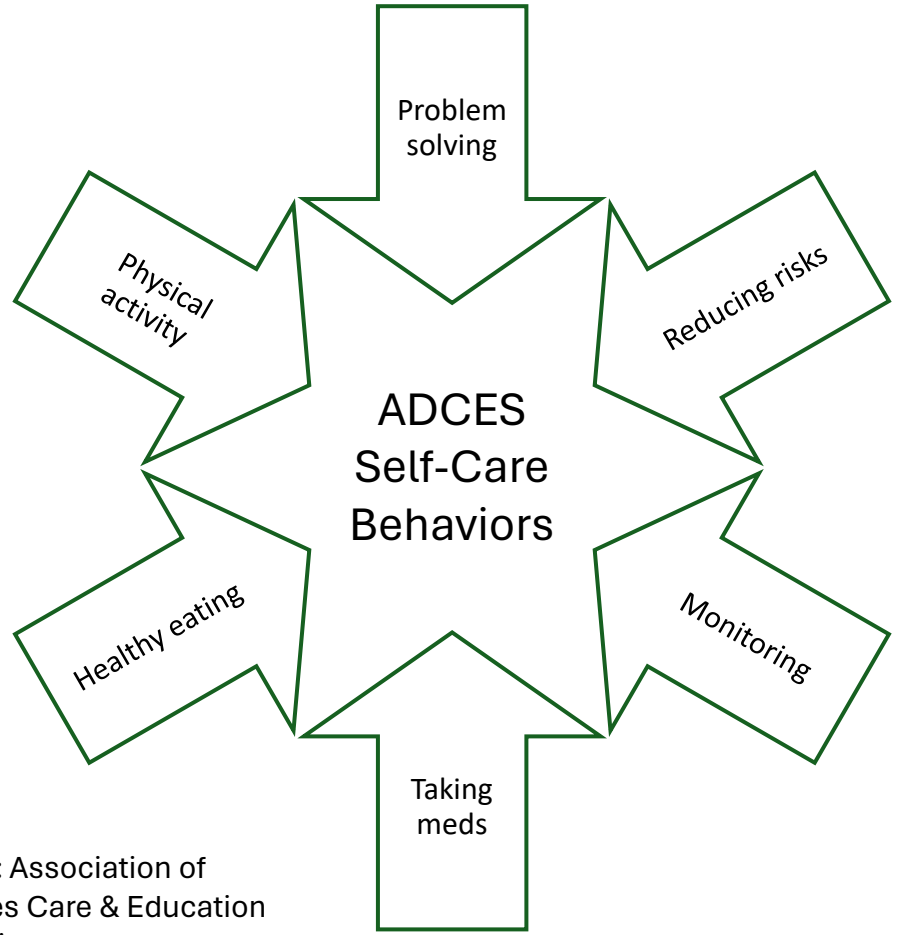
Diabetes Management



ADA. Standards of Care. 2024. Adapted from Figure 10.1.

DIABETES SELF MANAGEMENT EDUCATION & SUPPORT

What is it?



ADCES: Association of Diabetes Care & Education Specialists

- Lowers HbA1C by 0.45 - 0.57%
- Decrease complications and mortality
- Increases quality of life
- Increases self-efficacy and empowerment
- Improves coping skills
- Decreases emergency department visits, hospitalizations, and overall healthcare costs

ADA. Standards of Care. 2020.

DIABETES SELF MANAGEMENT EDUCATION & SUPPORT

When to refer patients to DSMES

Four critical times

- At diagnosis
- Annually or when not meeting treatment goals
- When complications occur
- When transitions in life/care occur

How to find a DSMES program

- ADCES website
- ADA website
- Group & individual visits available
- Telemedicine & interpreter services available

DSMES Insurance Coverage

Payer	Initial (10 hrs/yr)	Follow-up (~2 hrs/yr)
OH Medicaid	YES	YES
Medicare	YES	YES
Commercial	Varies; most cover	

ADA. Standards of Care. 2020.
ADCES. FAQ: Reimbursement. 2022.
Ohio Medicaid. Coverage and Payment for DSMT. 2021.

Medical Nutrition Therapy

- Emphasis has shifted to focus on dietary patterns vs. specific foods
- Not all carbohydrates are created equal. Reduce "spiky" carbs; increase "slow" carbs
- No specific macronutrient pattern specified; 25-30% of daily calories should be carbohydrate
- Reducing overall carbohydrate intake improves glycemia
- At minimum 20% of daily calories should be protein
- Limit saturated fats and replace with unsaturated fats (Mediterranean Diet)

How to find an MNT program

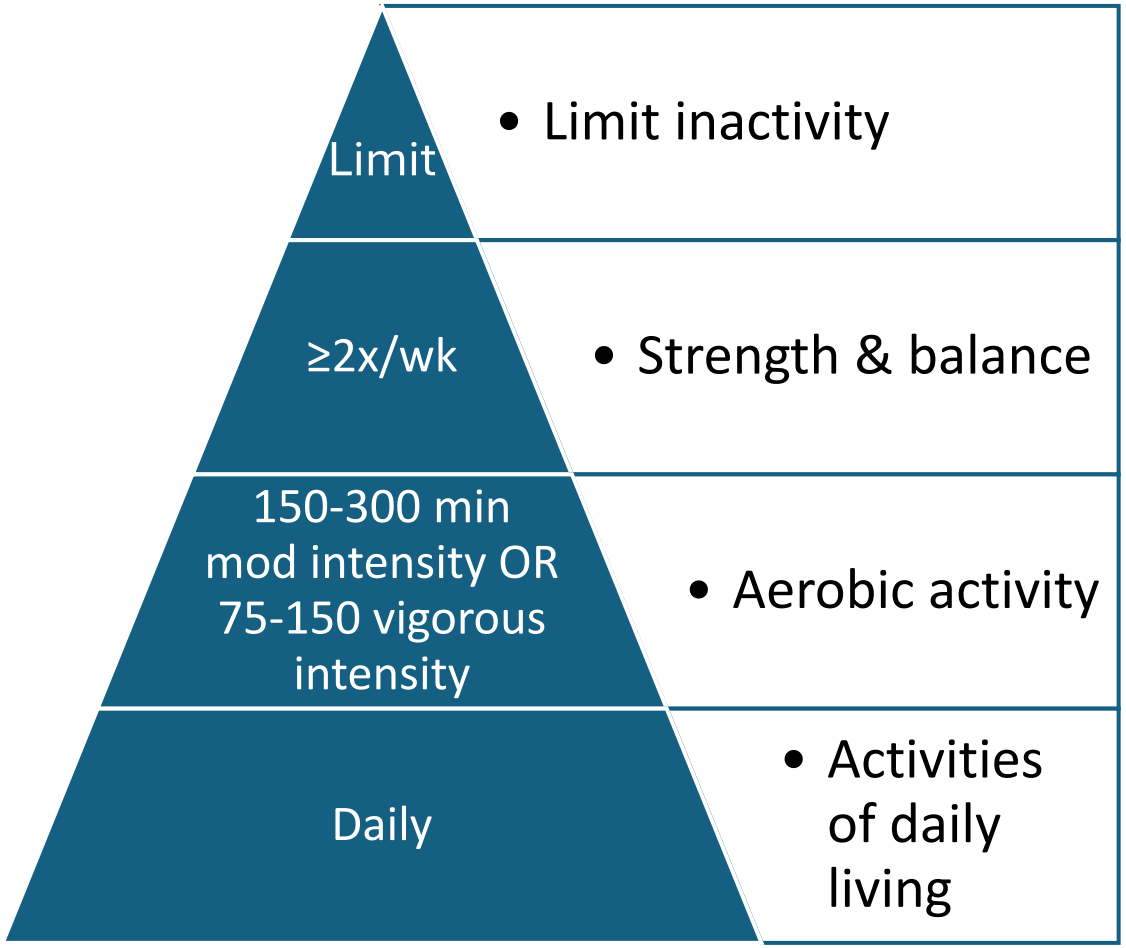
- Academy of Nutrition & Dietetics website
- Most health systems offer this service
- In person vs. telemedicine available

MNT Insurance Coverage

Payer	Coverage
OH Medicaid	YES
Medicare	YES
Commercial	Varies; most cover

ADA. Standards of Care. 2024
DiaTribe Learn. 42 Factors that affect glucose. 2022
OAND. MNT Coverage. 2022.

Physical Activity



- Losing weight + building muscle = less insulin resistance
- Increase in steps of ≥ 500/day, reduces CV risk
- Adding small levels of activity can reduce HbA1C
- Strength training + cardio is better than cardio alone
- Physical activity reduces stress and improves sleep

Where should patients start?

- Physical therapy
- Insurance covered programs
- Wellness initiatives
- Online videos
- Mobile apps

MU Dept of Nutritional Sciences. My Activity Pyrramid for Adults. 2023
DiaTribe. Diet and Exercise. 2023
ADA. Standards of Care. 2024

Technology

- Blood glucose monitors
- CGM
- Injection pens
- Insulin pumps
- Automated Insulin Delivery Systems (AIDS)
- Mobile coaching services

Blood Glucose Monitor Updates

- Bluetooth enabled devices send data to apps on mobile devices
- Apps can provide information on data including goals, trends, and motivational messaging
- Monitor and apps can be linked to online or phone diabetes coaching

ADA. Standards of Care. 2024
DiaTribe. Diabetes Devices. 2020.

Continuous Glucose Monitors

FDA Approved Personal Devices

- Abbott Freestyle 14 day, 2, and 3
- Dexcom G6, G7, Stela
- Medtronic Guardian 3, 4
- Senseonics Eversense

How to Incorporate Into Your Workflow

- Ensure adequate time is schedule for CGM education
- Encourage patients to use CGM for at least 14 days to see glucose patterns and trends
- Use trends & patterns to make lifestyle and/or medication adjustments

Appropriate for all patients with diabetes

Allows patients to play an active role in their diabetes care

Provides real time feedback on how medications, foods, exercise, stress, work, sleep etc. affect glucose

Empowers patients to make positive lifestyle changes

Payer	Coverage
OH Medicaid	YES; all pts with DM
Medicare	YES; 1 insulin injection/day OR hypoglycemia
Commercial	Varies

AACE. Guide to CGM. 2023

CGM Updates

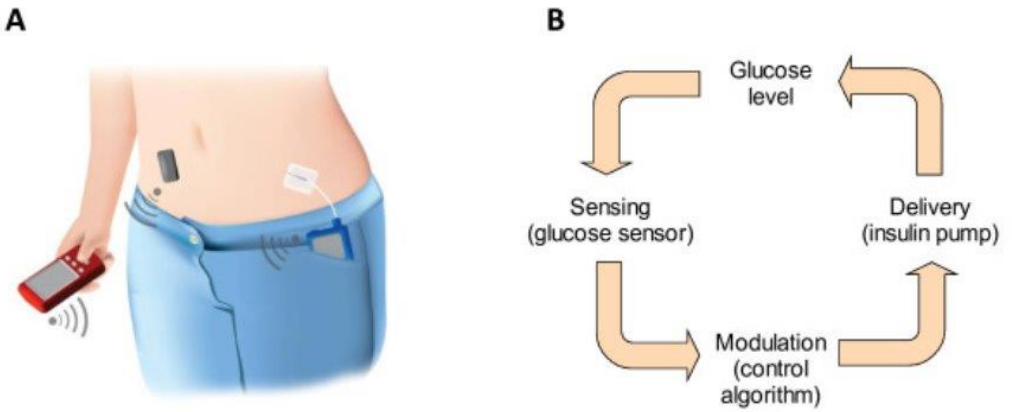
Device	Type	Approved Ages & Location	Frequency of BG checks	Sensor Life	Clinical Pearls	Availability
Dexcom Stelo (sensor + mobile app) APPROVED 3/5/24	Real-time CGM	Adults age ≥18 years Not on insulin Do not have problematic hypoglycemia Worn on back of upper arm	Every 15 minutes	15 days	Will exclude alerts & alarms geared towards insulin users Short warm up period	OTC! Anticipated Summer 2024
Accu-Chek SmartGuide	Real-time CGM	NOT approved	Undisclosed	14 days	Uses predictive artificial intelligence to determine where glucose may go Requires initial calibration	Currently an "investigational device"

www.dexcom.com/stelo

Drug Delivery Business. Accu-chek SmartGuide. 2024.

Automated Insulin Delivery Systems (AIDS)

- Improves Time in Range (TIR)
- Improvement in TIR overnight (protection from overnight hypoglycemia)
- Increased % of patients with HbA1C < 7%
- Reduces frequency of diabetic ketoacidosis hospitalizations
- Increase in TIR of 2.6 hours/day
- Reduce hypoglycemia and time below range



Eller D, et al. BMC.2011;9:120.

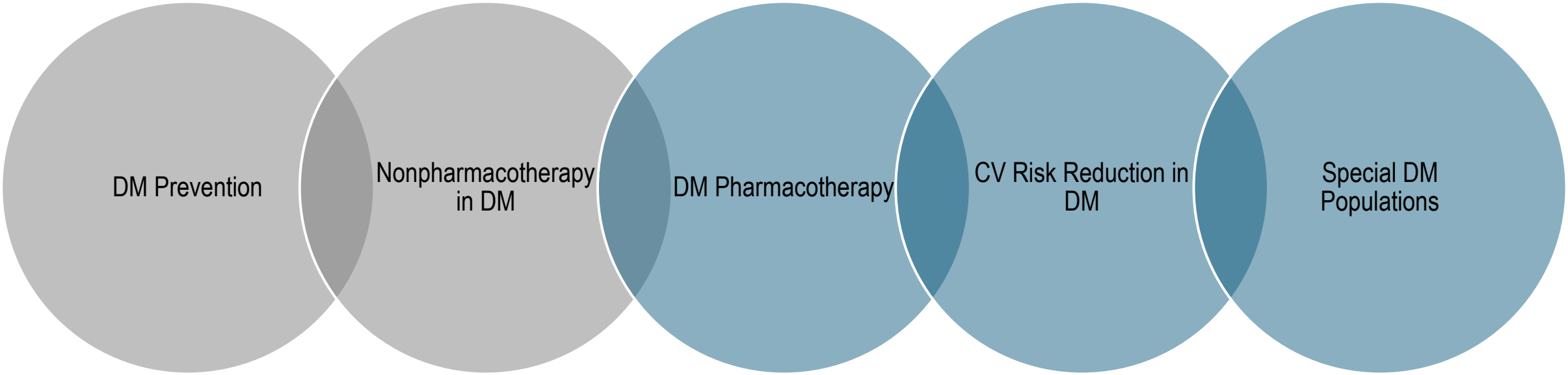
Diabetes Type	Coverage
T1DM	YES
T2DM	YES; generally requires ≥ 3 injections/day

ADA.Automated Insulin Delivery. 2022.

Patient Case 1 - Nonpharmacotherapy

- JS is a 55-year-old male
- PMH: T2DM (6 years), Hypertension (HTN) (5 years), Dyslipidemia (7 years), Depression (3 years)
- HPI: interested in improving lifestyle to improve his health but is overwhelmed by stressful work environment and busy schedule
- Social History: Married, works full time, adult children
- Family History: Father – T2DM (death post myocardial infarction; Mother – HTN, stroke
- Current medications: metformin 1000 mg BID, valsartan 160 mg daily, atorvastatin 20 mg daily, sertraline 50 mg daily
- Vitals: BP 124/72 mmHg, HR 70 bpm
- Labs: HbA1C 7.4%, LDL-C 64 mg/dL, Basic metabolic panel (BMP) within normal limits (WNL), Patient Health Questionnaire-9: 3

Topic Map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PHARMACOTHERAPY UPDATES

T1DM Pharmacotherapy Updates

Medication	Dose	MOA	Side Effects	Warnings
Teplizumab-mzwv Delay onset of symptomatic stage 3 T1DM in age ≥ 8yo with presymptomatic stage 2 T1DM.	2mg/2mL vial. 30 min IV infusion using BSA based dosing once daily for 14 days	Binds CD3 (cell surface antigen on T lymphocytes) - may result in partial agonistic signaling and deactivation of pancreatic beta cell autoreactive T lymphocytes.	Lymphopenia, rash, leukopenia, headache, increased ALT, nausea, diarrhea, nasopharyngitis	Cytokine release syndrome, serious infections, lymphopenia, hypersensitivity reactions, vaccinations (administer all age-appropriate vaccines prior to use)

Medication	Dose	MOA	Side Effects	Warnings
Donislecel T1DM + level 3 hypoglycemia despite intensive education	Single infusion into the hepatic portal vein. An additional infusion may be performed if needed	Secretion of insulin via infused allogenic beta cells	Opportunistic infections, procedure complications, infusion reaction	Concomitant immunosuppression required

Tzield. Package Insert. 2022.
Latindra. Package Insert. 2024

T2DM Pharmacotherapy Updates

Medication	Dose	HbA1C Lowering + Weight Loss	MOA	Side Effects	Warnings	Monitoring
Tirzepatide	2.5-15 mg SQ once weekly	~2.0-2.3% HbA1C lowering 12.8-14.7% (placebo 3.2%) Weight loss	GLP-1 RA/GIP Selectively binds and activates both GIP and GLP-1 receptors.	Nausea, diarrhea, deceased appetite, vomiting, constipation, dyspepsia, abdominal pain	Thyroid c-cell tumors, pancreatitis, severe GI disease, diabetic retinopathy complications (with retinopathy history), acute gallbladder disease	ADEs Glucose Hypoglycemia (when used with other agents) Weight

Medication	Dose	HbA1C Lowering	MOA	Side Effects	Monitoring
Bexagliflozin	20 mg by mouth daily	~0.7-1.0%	Inhibition of SGLT2 co-transporter reducing renal reabsorption of filtered glucose and increasing urinary glucose excretion	Genital fungal infections, urinary tract infection, ketoacidosis, dizziness, hypotension, increased LDL, increased urination low risk of hypoglycemia, amputations	ADEs Hypoglycemia Weight loss Blood pressure Renal function

Mounjaro. Package insert. Lilly. 2022.
Brenzavvy. Package insert. Theracos Bio. 2023

T2DM Management

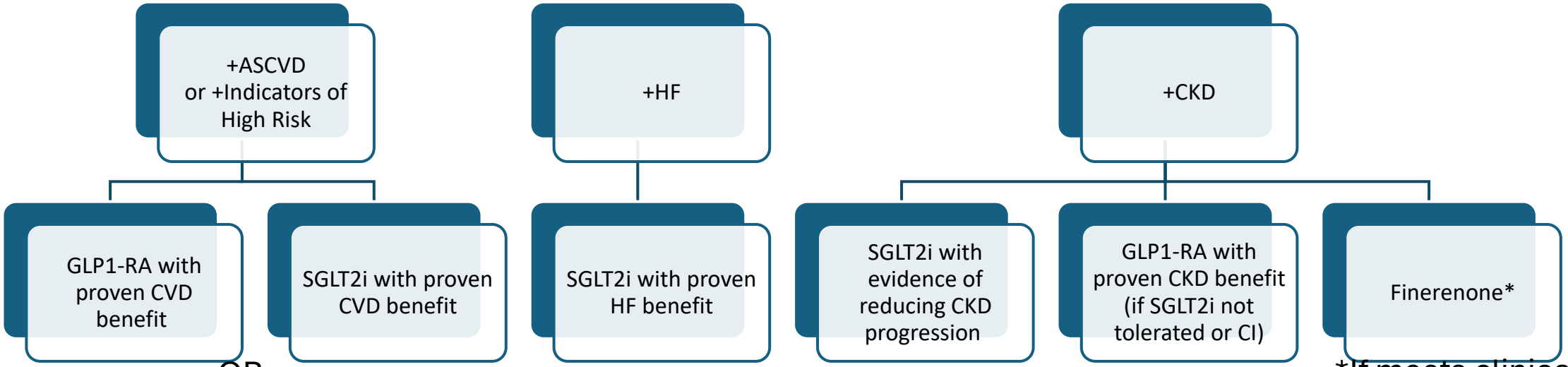
Healthy lifestyle behaviors, DSMES and address SDOH

Goals

ADA. Standards of Care. 2024.

Goal: Cardiorenal Risk Reduction in High-Risk Individuals

ASCVD: Atherosclerotic Cardiovascular Disease
CI: contraindicated
HF: Heart Failure



*If meets clinical criteria

ADA. Standards of Care. 2024.
Marx N. *Euro Heart J*.2023. 44(39):4043-4140.

Goal: Achievement and Maintenance of Glycemic and Weight Management

Efficacy for Glucose Lowering

- Very High: dulaglutide, semaglutide, tirzepatide, insulin, combination oral or injectable (GLP1-RA/insulin)
- High: GLP-1 RA (not listed in very high), metformin, SGLT2i, sulfonylurea, thiazolidinediones (TZD)
- Intermediate: Dipeptidyl peptidase IV inhibitor (DPP-4i)

Efficacy for Weight Loss

- Very High: semaglutide, tirzepatide
- High: dulaglutide, liraglutide
- Intermediate: GLP-1 RA (not listed above), SGLT2i
- Neutral: DPP-4i, metformin

ADA. Standards of Care. 2024.

Injectable Therapy for T2DM

1. • Consider GLP1-RA or dual GIP/GLP1-RA in most patients prior to insulin
2. • Add basal insulin if above target
3. • Add prandial insulin

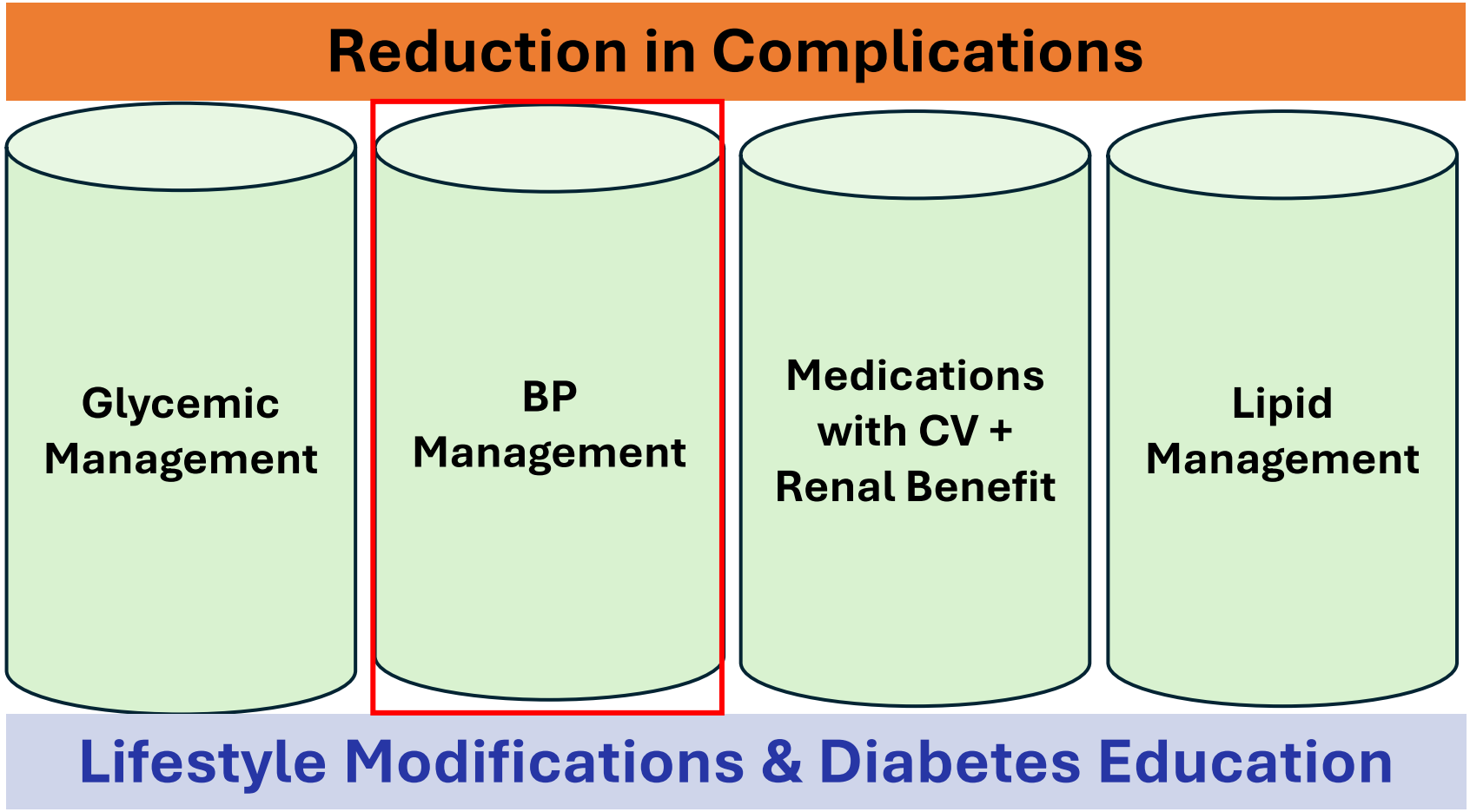
ADA. Standards of Care. 2024.

Patient Case 2 - Pharmacotherapy

- MR is a 48-year-old female
- PMH: T2DM (4 years), HTN (3 years), Asthma (40 years)
- HPI: Concerned with fatigue, increased thirst and current weight
- Social History: Married with two teenage children, works full time
- Current medications: budesonide/formoterol 4.5/80 mcg as needed, lisinopril 10 mg daily
- Vitals: BP 120/68 mmHg, HR 78 bpm, BMI 30kg/m2
- Labs: HbA1C 9.0%, BMP WNL, Urine Albumin Creatinine Ratio (UACR) 13

CARDIOVASCULAR RISK REDUCTION IN DIABETES

Diabetes Management



ADA. Standards of Care. 2022

HTN + Blood Pressure Control

HTN = risk factor for ASCVD + microvascular complications

Check BP every visit

HTN is systolic BP (SBP) ≥ 130 or diastolic BP (DBP) ≥ 80 mmHg

All patients should monitor BP at home

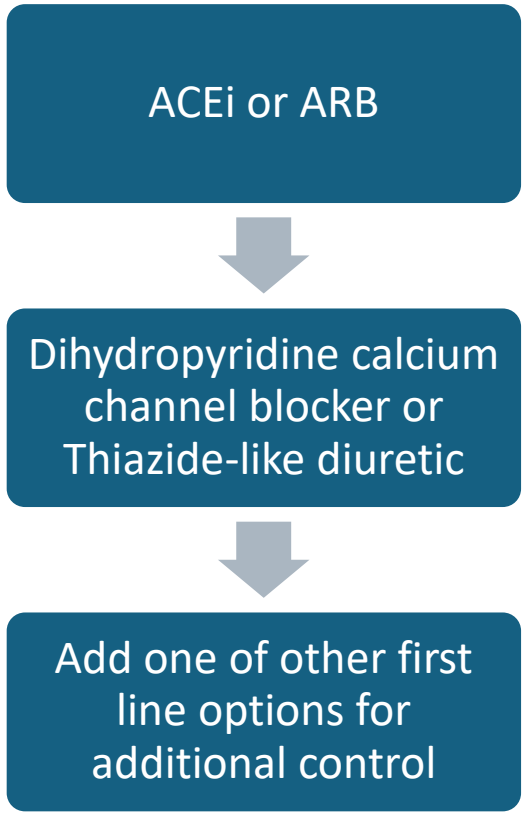
Goal BP ≤ 130/80 mmHg

ADA. Standards of Care. 2024.

HTN Treatment

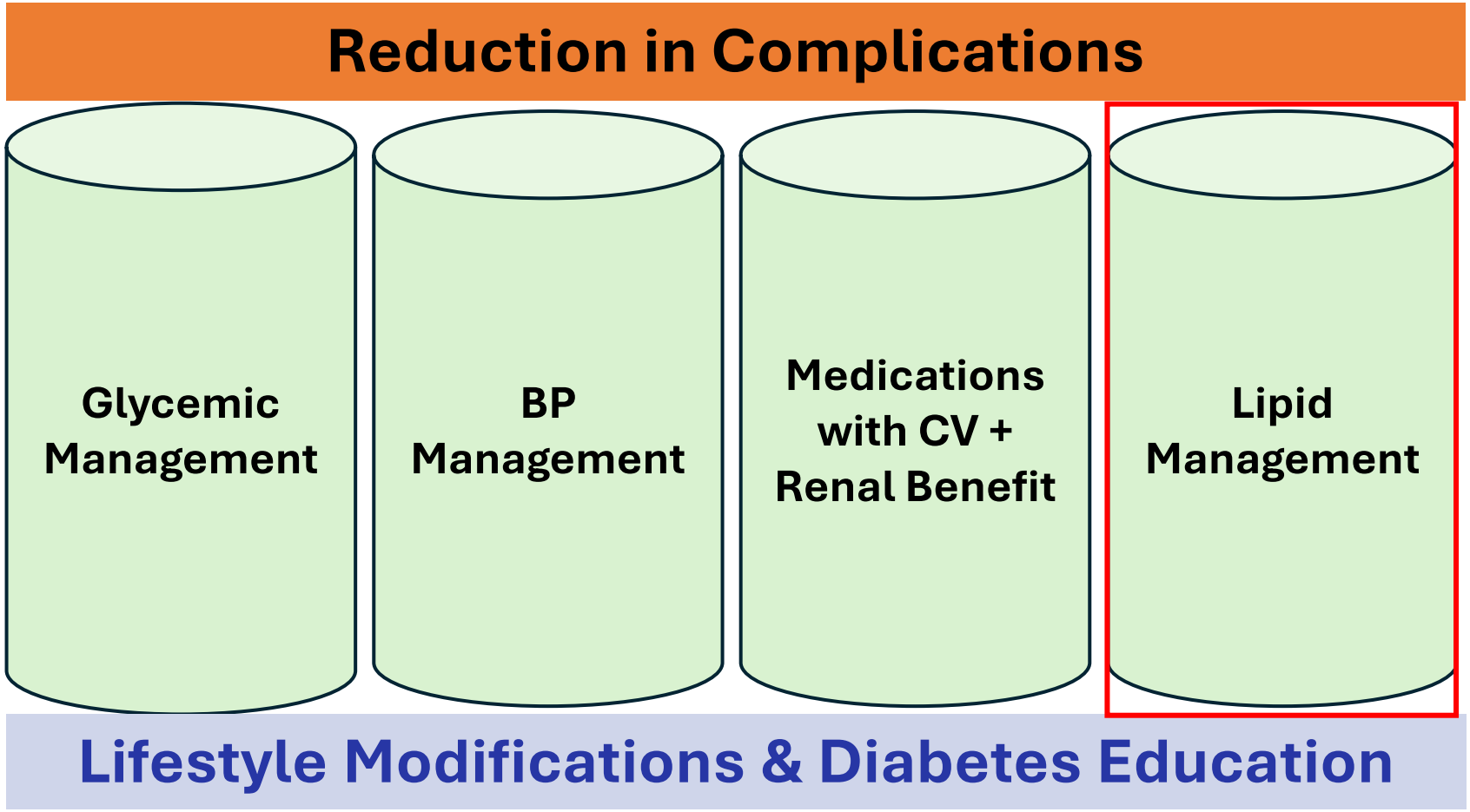
- Lifestyle Interventions
  - DASH diet: Reducing sodium and increasing potassium
    - Sodium restriction = SBP reduction ~2-8 mmHg
  - Alcohol moderation
  - Smoking cessation
  - Increased physical activity = SBP reduction ~2-9 mmHg
  - Weight loss: 10kg = SBP reduction ~5-20 mmHg

- Pharmacological Interventions



ADA. Standards of Care. 2024.
US HHS. JNC 7. Hypertension. 2003.

Diabetes Management



ADA. Standards of Care. 2022.

Lipid Management

- Lifestyle Interventions
  - Weight loss (if indicated)
  - Mediterranean or DASH diet
  - Reduced saturated fat and trans fat
  - Increase dietary n-3 fatty acids, viscous fiber, and plant stanols/sterols
  - Increase physical activity
- Monitoring – lipid panels
  - At diagnosis of pre-diabetes or diabetes (not on lipid-lowering therapy)
  - 4-12 weeks after initiation of therapy or dose adjustments
  - Annually thereafter (or more frequent if indicated)

- Four Patient Management Groups

Primary Prevention	Secondary Prevention
• Adults with LDL ≥ 190 mg/dL • **Adults with diabetes** • Adults without diabetes	• **Adults with clinical ASCVD**

ADA. Standards of Care. 2024.
Lloyd-Jones, et al. J Am Coll Cardio. 2022

Lipid Management

Primary Prevention

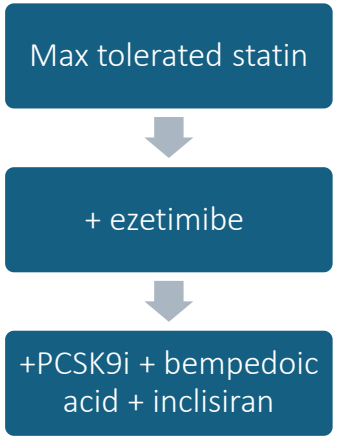
- Calculate ASCVD Risk + Assess
- 20-39 years old + DM = consider statin with additional risk factors
- 40-75 years old + DM = moderate or high intensity statin (based on risk)
- >75 years old + DM = Can continue if on a statin or initiate moderate intensity

Low-density lipoprotein (LDL) goals

- ≤ 70 or ≤ 100 mg/dL

LDL % reduction goal

- 30 – ≥ 50% baseline



Secondary Prevention

- All ages + DM + ASCVD = high intensity statin

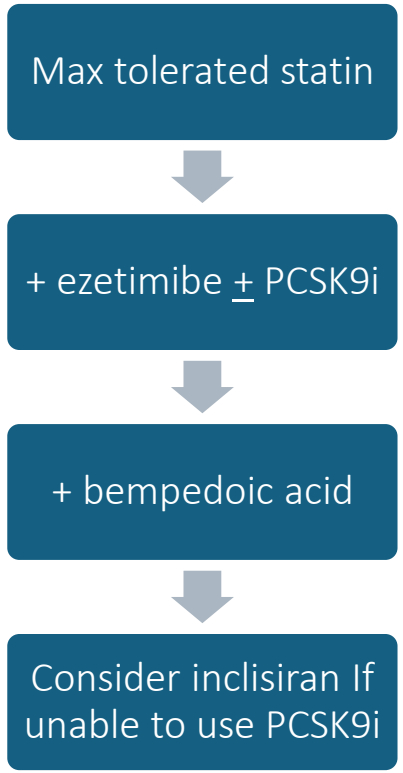
LDL goals

- ≤ 55** or ≤ 70 mg/dL

LDL % reduction goal

- ≥ 50% baseline

** Lower goal for very high risk = Hx of multiple ASCVD events OR 1 major ASCVD event + multiple high-risk conditions



ADA. Standards of Care. 2024.
Lloyd-Jones, et al. J Am Coll Cardio. 2022

Antiplatelet Agents

Secondary Prevention

- DM + ASCVD = aspirin 81 mg daily
- Use clopidogrel 75 mg if documented aspirin allergy

Acute Coronary Syndrome

- Dual antiplatelet therapy indicated after ACS and coronary revascularization with stenting or ischemic stroke/transient ischemic attack
- Duration determined with interprofessional team
- Long term use of dual antiplatelet therapy consider with prior coronary intervention, high ischemic risk and low bleeding risk

Stable Coronary or Peripheral Artery Disease

- Consider low-dose rivaroxaban + aspirin

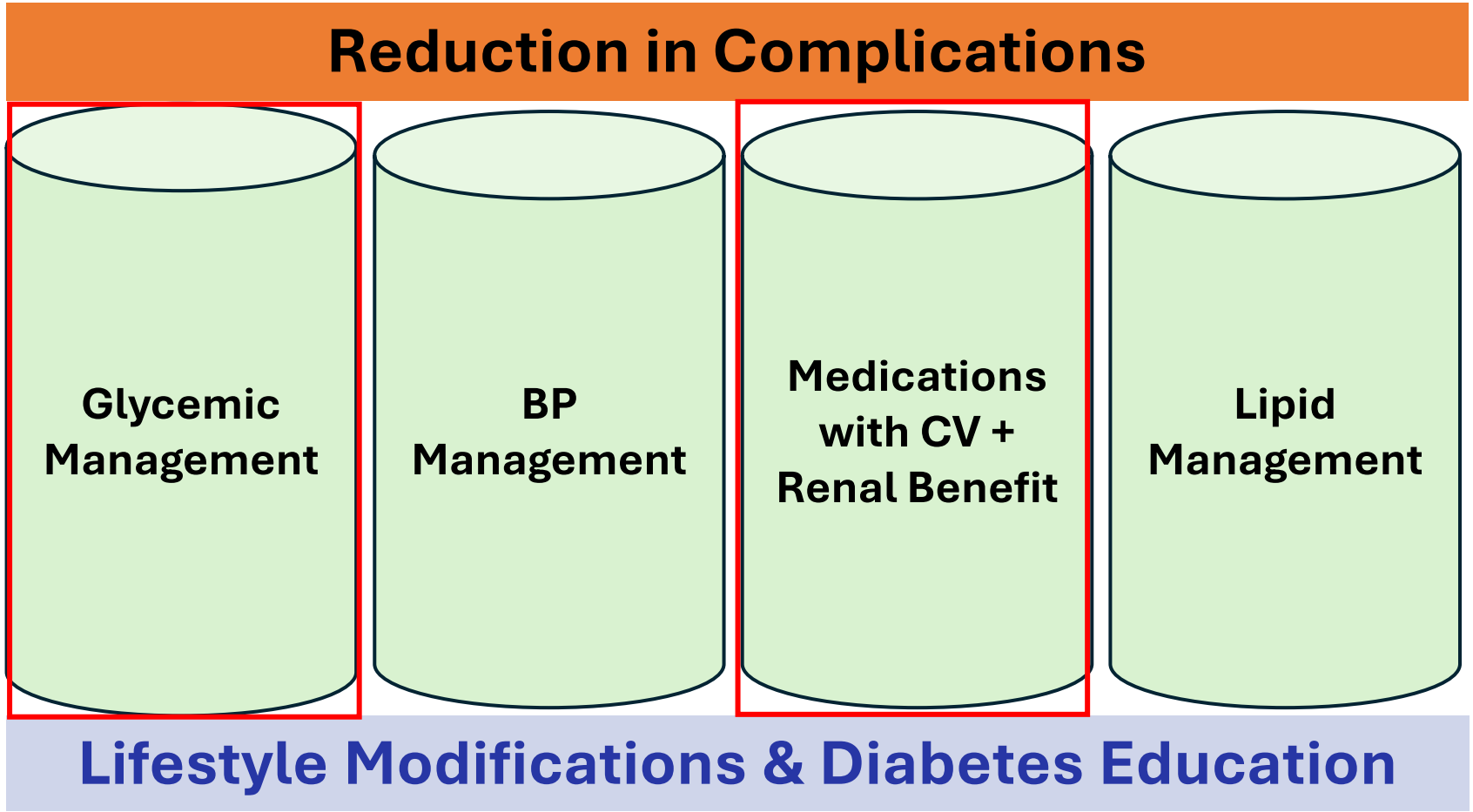
ADA. Standards of Care. 2024.

Aspirin for Primary Prevention

Population	Recommendation
Adults 40-59 years with ASCVD risk ≥ 10%	Individual review of risk vs benefit. Net benefit small. Patients not at increased risk of bleeding who are willing to take aspirin are more likely to benefit.
Adults ≥ 60 years	Not recommended for initiation
Adults ≥ 75 years	Consider stopping aspirin

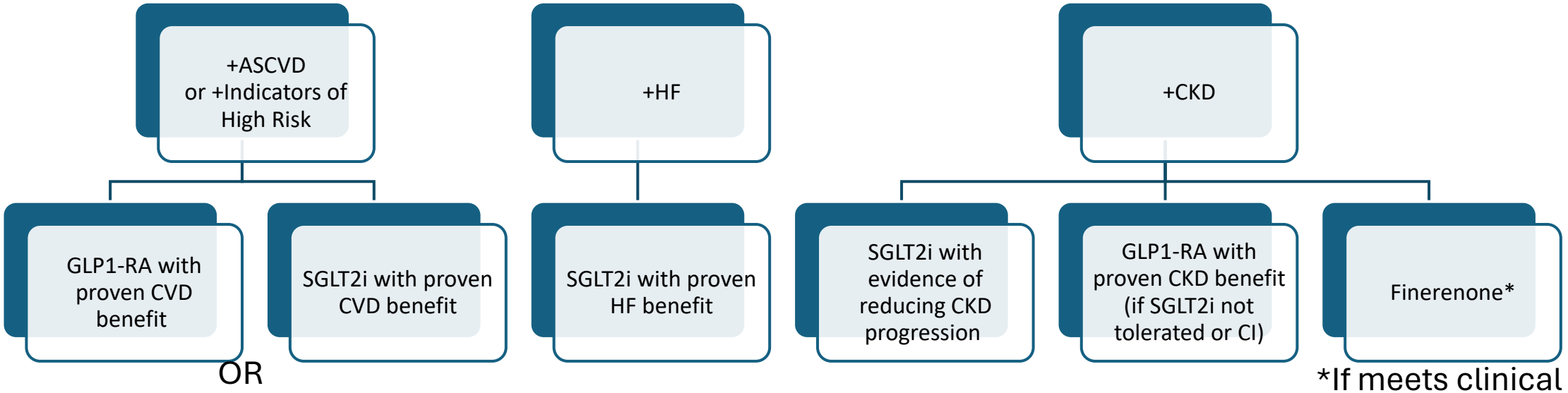
Aspirin use. USPSTF. 2022.

Diabetes Management



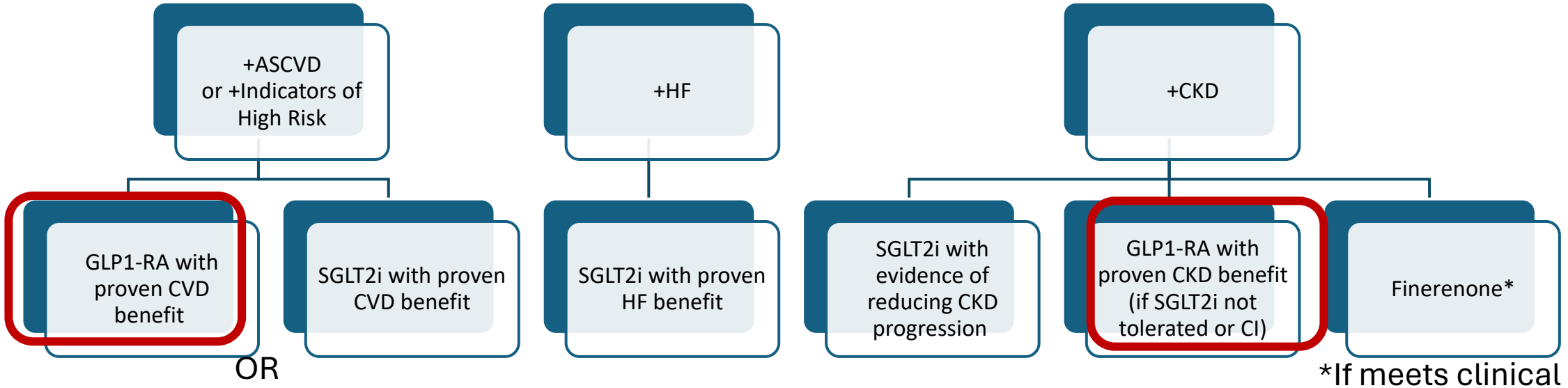
ADA. Standards of Care. 2022.

Cardiorenal Risk Reduction in High-Risk Individuals



ADA. Standards of Care. 2024.
Marx N. *Euro Heart J*.2023. 44(39):4043-4140.

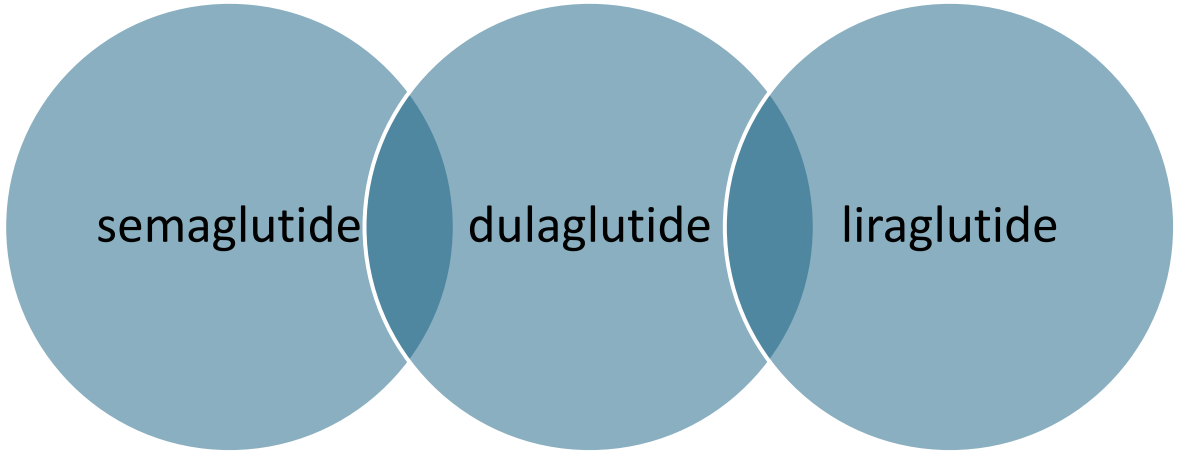
Cardiorenal Risk Reduction in High-Risk Individuals



ADA. Standards of Care. 2024.
Marx N. *Euro Heart J*.2023. 44(39):4043-4140.

CV and Renal Benefit – GLP1-RAs

HbA1C lowering: ~1.5%



CV Trial

2019: PIONEER-6 (semaglutide)

Renal Trial

2023: FLOW (semaglutide)

CV + Renal Trials

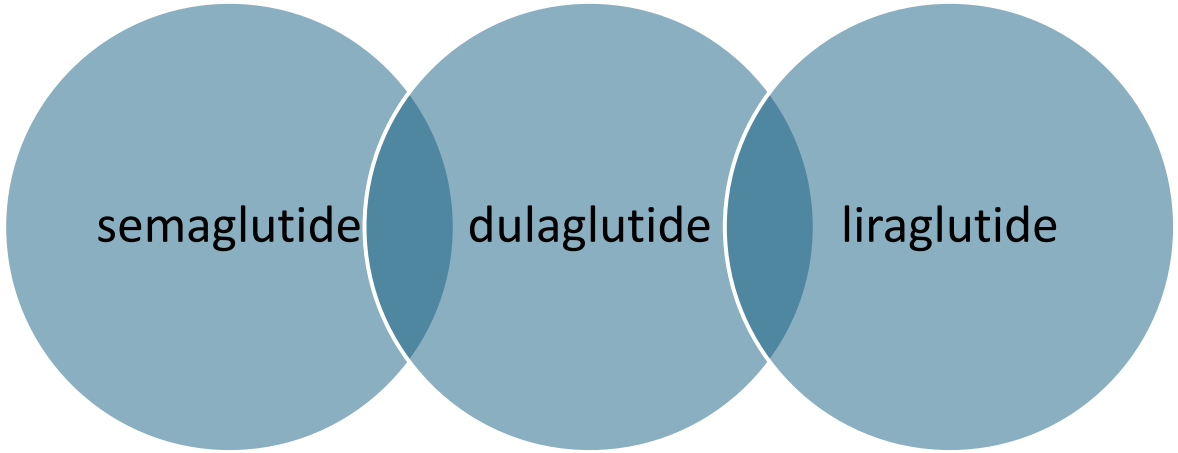
2016: LEADER (liraglutide)
2016: SUSTAIN (semaglutide)
2019: REWIND (dulaglutide)

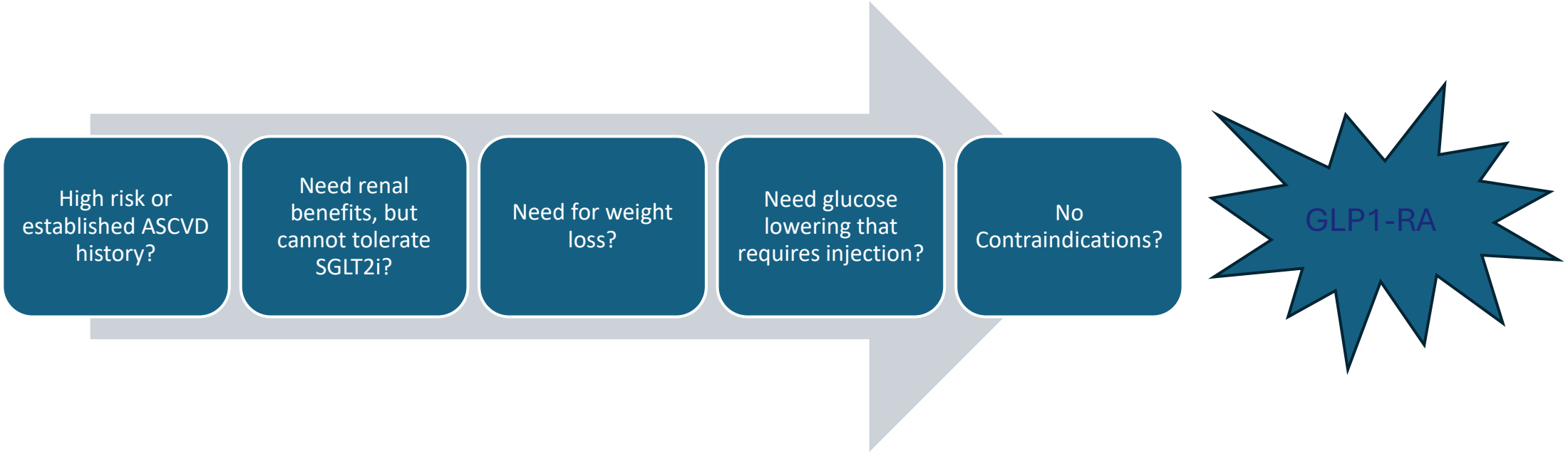
Practice Pearls

- Oral semaglutide must be taken on an empty stomach with ≤ 4 oz of water and 30 min before eating, drinking, or other meds
- GI effects can be minimized through proper patient education
- Ensure patients have pen needles if appropriate

ADA. Standards of Care. 2024.

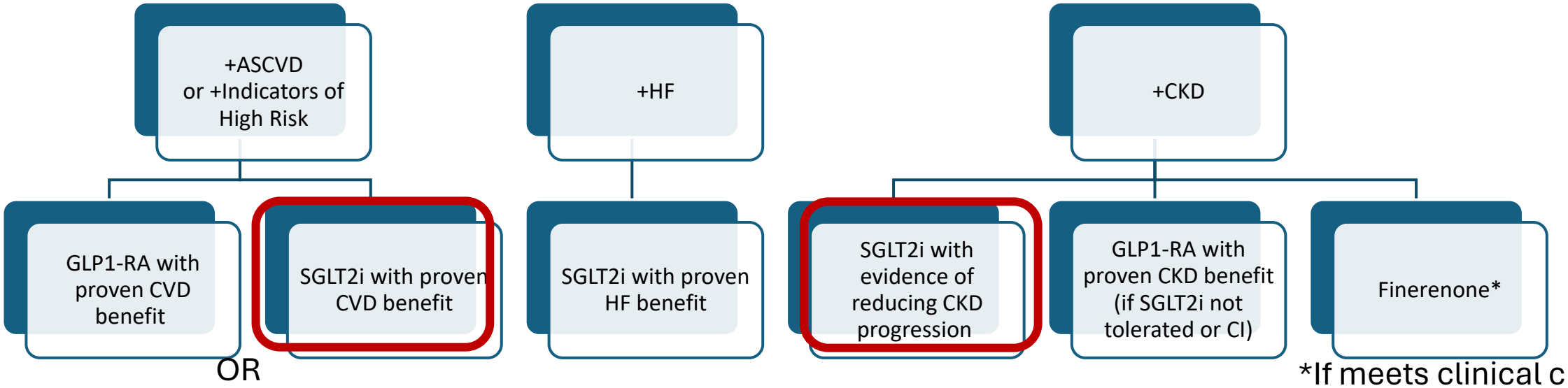
CV and Renal Benefit – GLP1-RAs





ADA. Standards of Care. 2024.

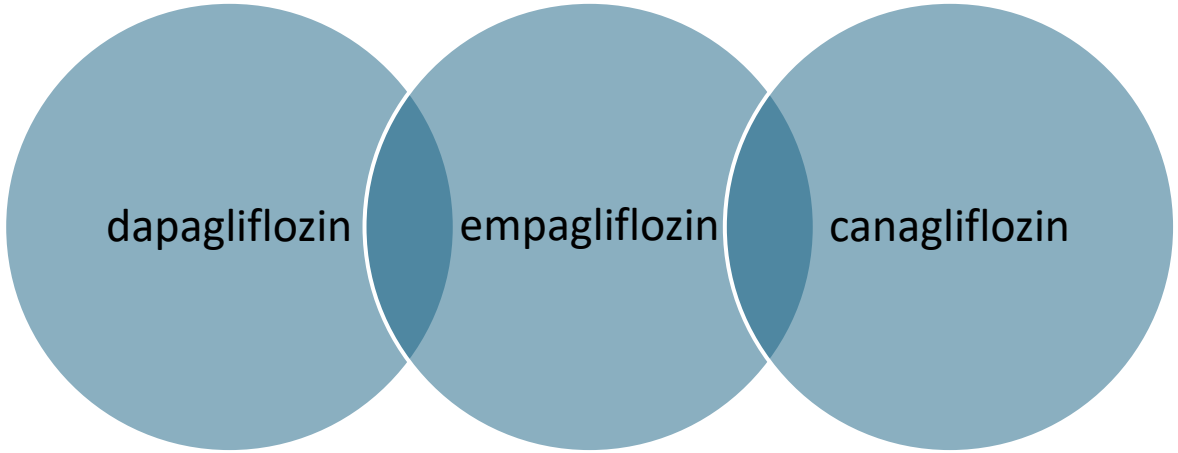
Cardiorenal Risk Reduction in High-Risk Individuals



ADA. Standards of Care. 2024.
Marx N. *Euro Heart J*.2023. 44(39):4043-4140.

CV and Renal Benefit – SGLT2is

HbA1C lowering: 0.7-1%



CV Trials

2015: EMPA-REG (empagliflozin)
2015: CANVAS (canagliflozin)
2019: DECLARE TIMI 58 (dapagliflozin)

Renal Trials

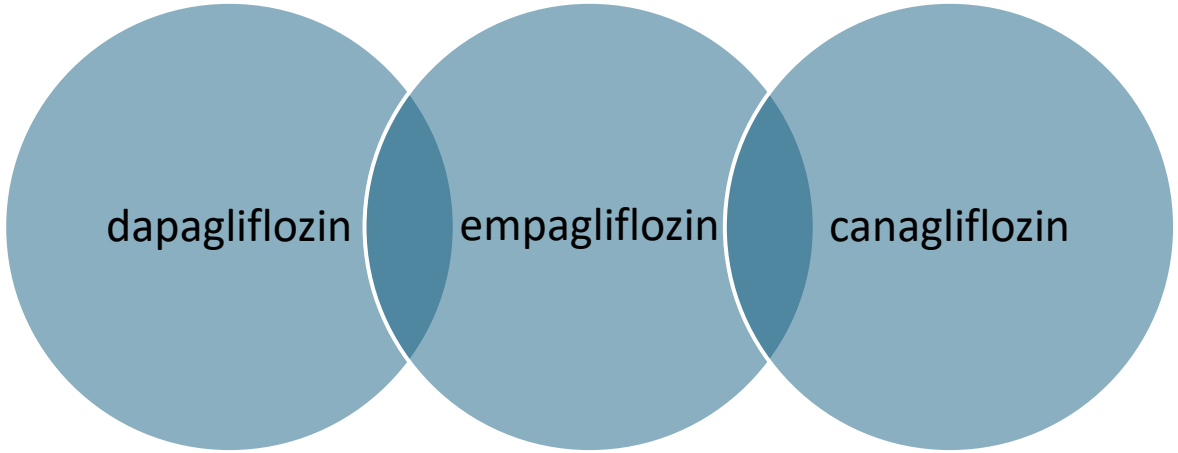
2017: CANVAS-R (canagliflozin)
2019: CREDENCE (canagliflozin)
2021: DAPA CKD (dapagliflozin)
2022: EMPA-KIDNEY (empagliflozin)

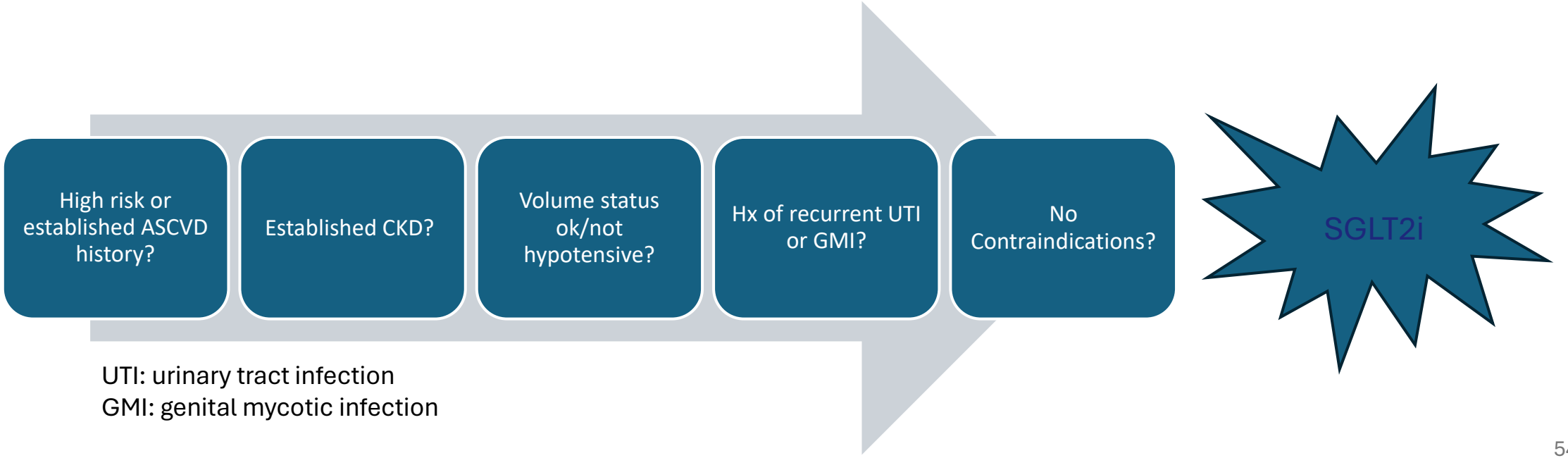
Practice Pearls

- Review volume status and BP prior to initiation
- Monitor basic metabolic panel in 2-4 weeks following initiation or dose adjustment
- Cannot be used in patients with T1DM
- Encourage patients to stay well hydrated when initiating therapy

ADA. Standards of Care. 2024.; Perkovic, et al. NEJM. 2019.; Heerspink, et al. NEJM. 2020.; Herrington, et al. NEJM. 2023.; Zinman, et al. NEJM 2018.; Neal, et al. NEJM. 2017.; Wiviott, et al. NEJM, 2019.

CV and Renal Benefit – SGLT2is

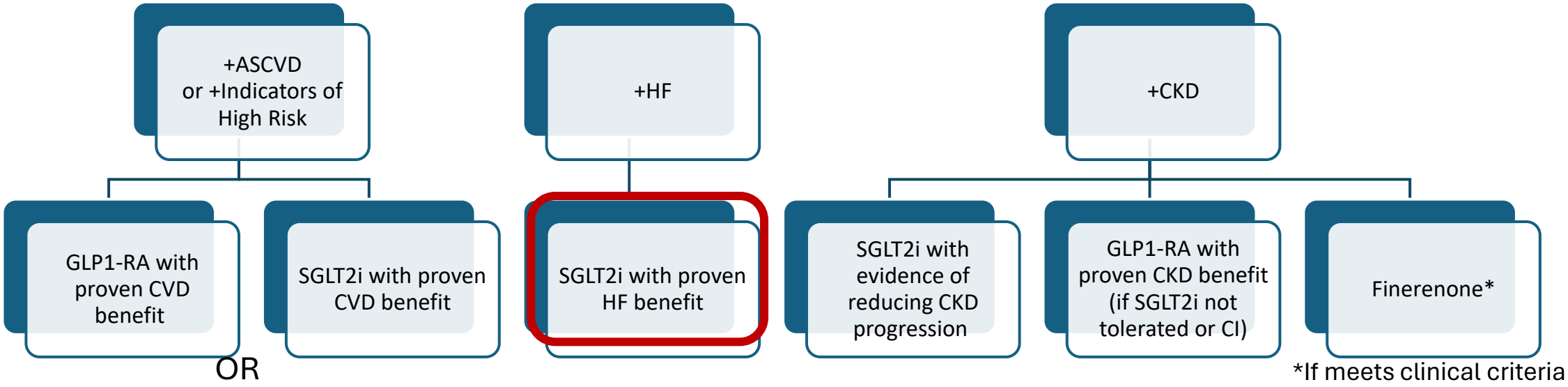




UTI: urinary tract infection
GMI: genital mycotic infection

ADA. Standards of Care. 2024.

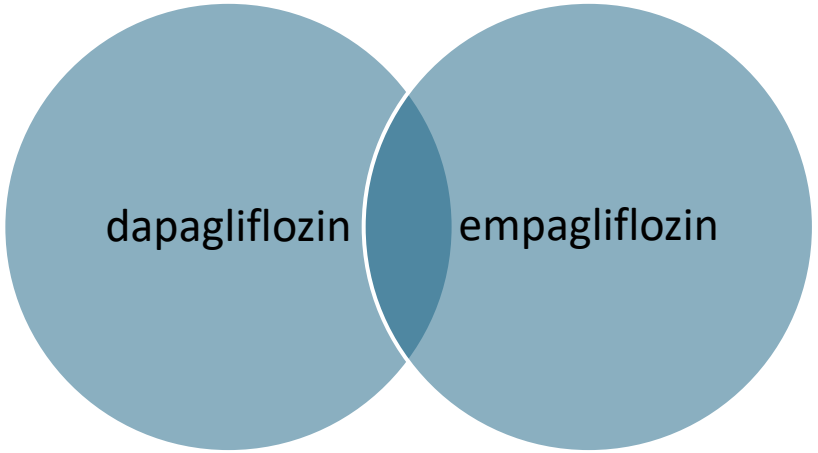
Cardiorenal Risk Reduction in High-Risk Individuals



ADA. Standards of Care. 2024.
Marx N. *Euro Heart J*.2023. 44(39):4043-4140.

HF Benefit – SGLT2is

HFrEF: Class 1A recommendation



HFpEF: Class 2A recommendation

HFrEF Trials

2019: DAPA HF (dapagliflozin)

2020: EMPEROR REDUCED (empagliflozin)

HFpEF Trials

2021: EMPEROR PRESERVED (empagliflozin)

2022: DELIVER (dapagliflozin)

HFrEF: Heart Failure Reduced Ejection Fraction

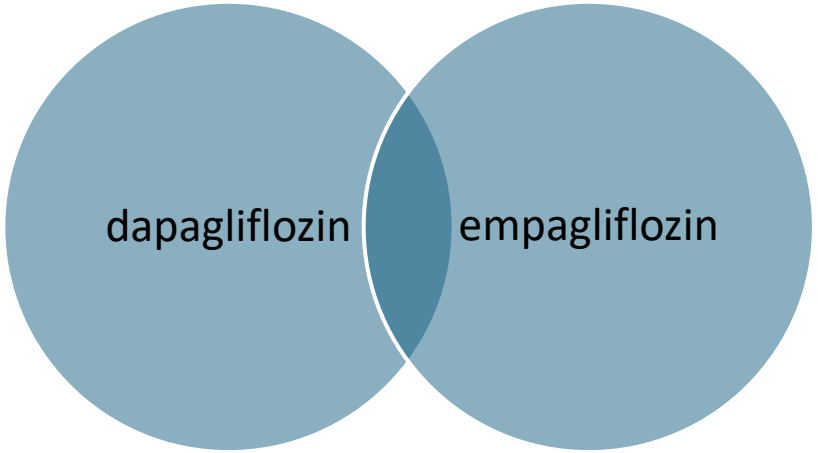
HFpEF: Heart Failure Preserved Ejection Fraction

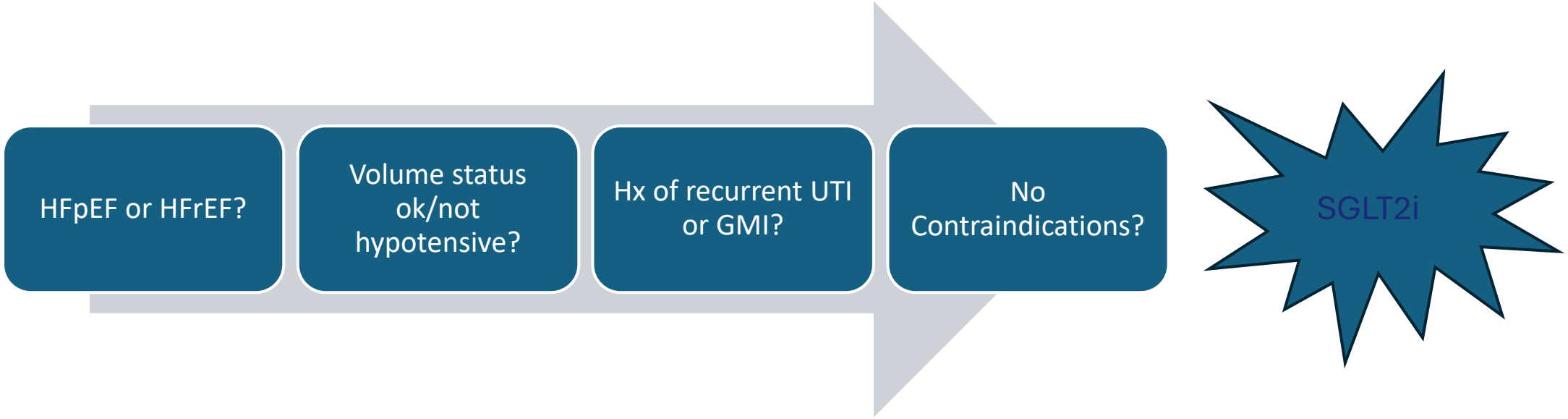
Practice Pearls

- Approved for use in patients ± DM
- Cannot be used in patients with T1DM
- Review volume status and BP prior to initiation
- Monitor BMP in 2-4 weeks following initiation or dose adjustment
- Encourage patients to stay well hydrated when initiating therapy

ADA. Standards of Care. 2024.; ACC/AHA. Guidelines on Heart failure. 2023.; McMurray, et al. NEJM. 2019.; Packer, at al. NEJM. 2020.; Solomon, et al. NEJM. 2022.;

HF Benefit – SGLT2is





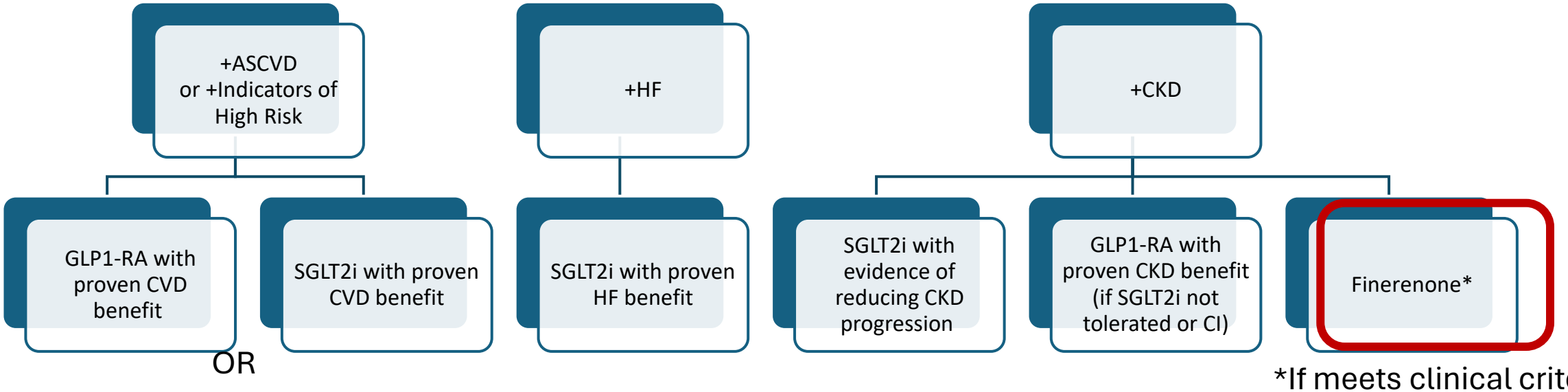
ADA. Standards of Care. 2024.

STEP-HFpEF Trial

Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity	
Population	529 patients with HFpEF and BMI ≥30kg/m2 followed for 52 weeks
Methods	Semaglutide 2.4 mg SQ weekly vs placebo Primary End Point: change from baseline in Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS 0-100) Secondary End Points: 60 minute walk distance, hierarchical composite (death, HF events, differences in KCCQ-CSS + 6 min walk test, changes in c-reactive protein)
Results	•Mean change in KCCQ-CSS 16.6 points in semaglutide vs 8.7 points in placebo (P<0.001) •Mean change in 6 minute walk distance 21.5 m with semaglutide vs 1.2 m with placebo (P<0.001) •Hierarchical composite endpoint, semaglutide produced more wins than placebo (P<0.001) •Serious adverse events occurred in 13.3% in semaglutide group and 26.7% of placebo group
Takeaway	•In patients with HFpEF and obesity, treatment with semaglutide led to larger reductions in symptoms and physical limitations compared to placebo

Kosiborod MN, et al. N Engl J Med. 2023.

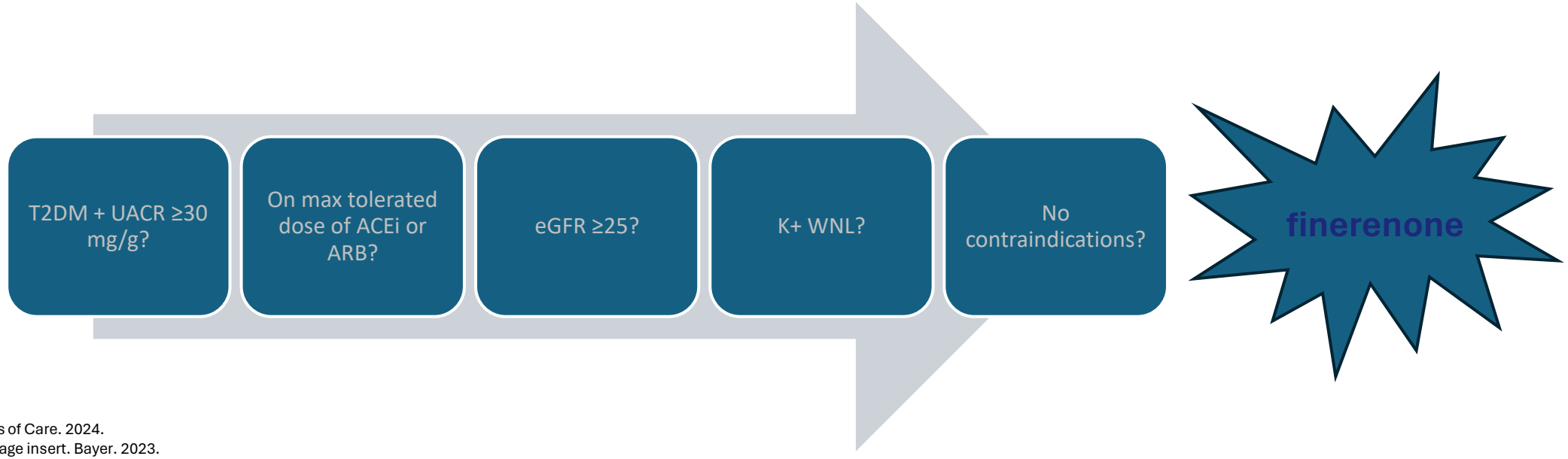
Cardiorenal Risk Reduction in High-Risk Individuals



ADA. Standards of Care. 2024.
Marx N. *Euro Heart J*.2023. 44(39):4043-4140.

– ns-MRA

Drug	Dose	MOA	Side Effects + Warnings	Monitoring	Cost
Finerenone *(Kerendia)*	10 – 20 mg once daily	Inhibits mineralocorticoid receptors No affinity or activity on androgen, progesterone, estrogen, or glucocorticoid receptors	CI: Strong CYP3A4 inhibitors, adrenal insufficiency ADRs: hypotension, hyperkalemia	BMP (including serum creatinine and potassium), BP	$$$



ADA. Standards of Care. 2024.
Kerendia. Package insert. Bayer. 2023.

Metformin and Pioglitazone

Metformin

- CV: Literature has supported beneficial effects in CVD, CV mortality, and CV protective effects
- Renal: KDIGO indicates initiation and use safe with eGFR ≥ 30
- HF: Possible mortality reduction in T2DM + stable HF. Avoid in hospitalized pts

Pioglitazone

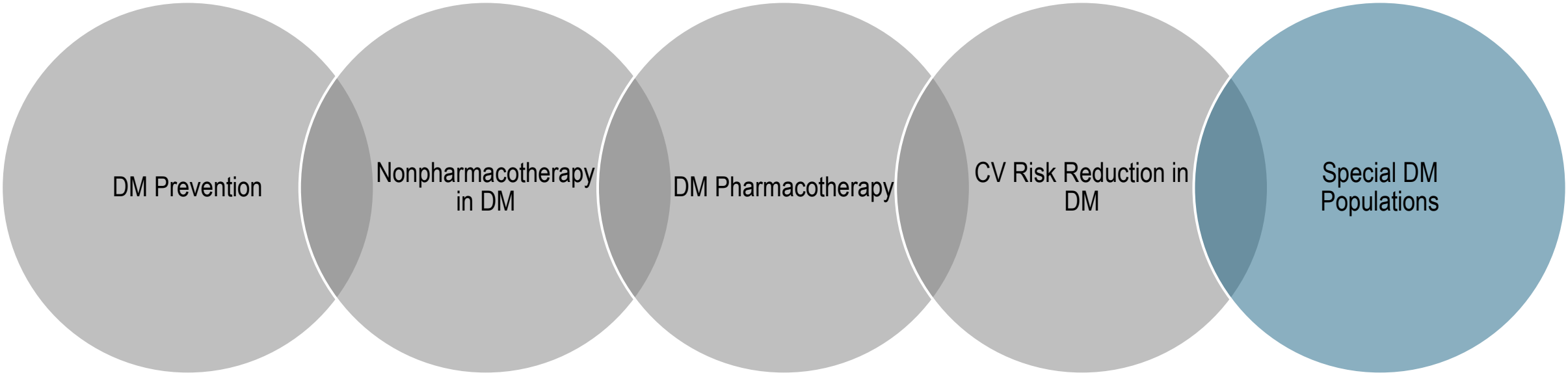
- CV: Benefit in patients with hx of stroke + prediabetes to reduce stroke and MI risk
- Renal: No specific benefit
- HF: CONTRAINDICATED

ADA. Diabetes Standards of Care. 2024.
Li JZ, et al. Cardiology. 2023.
Metformin. Package insert. Bristol Meyers Squibb. 2017.
Pioglitazone. Package insert. Takeda. 1999.
KDIGO Guidelines. 2022.

Patient Case 3 – Risk Reduction

- DC is a 64-year-old female
- PMH: T2DM (7 years), HTN (6 years), COPD (3 years)
- HPI: Here to establish care
- Social History: Single, recently moved to the area
- Current medications: umeclidinium/vilanterol 62.5mcg/25mg once daily, valsartan 320mg daily, metformin 1000mg BID, dulaglutide 1.5mg once weekly, albuterol HFA prn
- Vitals: BP 121/76 HR 68, BMI 27.8
- Labs: HbA1C 6.4%, UACR 187 mg/g, BMP WNL

Topic Map


DM Prevention
Nonpharmacotherapy in DM
DM Pharmacotherapy
CV Risk Reduction in DM
Special DM Populations

SPECIAL DIABETES POPULATIONS

T1DM

Insulin only (generally)

- Pramlinitide is FDA approved to reduce A1C
- Off label use of GLP1-RA to reduce insulin requirements
- SGLT2i not recommended (even in HF) due to DKA. T1DM excluded in trials

Early use of CGM recommended

AIDS use should be recommended

ADA. Standards of Care. 2024.

Older Adults

- HbA1C < 7% in patients with minimal comorbidities and high functional status
- HTN goals should be similar to general population
- CV risk reduction strategies may benefit those with life expectancies at least equal to the timeframe of the studies (2-6 years)
- De-intensity hypoglycemia causing meds & simplify regimen
- As life expectancy decreases, discuss goals and intensity of care with patients and families

ADA. Standards of Care. 2024.

Preoperative Management

For patients having elective surgery, it's recommended to do the following:

GLP1-RA

- Once daily agents: hold on the day of procedure
- Once weekly agents: hold one week prior to procedure

SGLT2i

- Hold 3 days prior to procedure

ASA. Task Force on Preperative Fasting. 2023
ADA. Standards of Care. 2024.

Pregnancy

- Preconception HbA1C goal ≤ 6.5% to reduce risk of fetal complications

HbA1C	≤ 6.0% (if possible) OR ≤ 7%
BGM Users	
Fasting BG	70 – 95 mg/dL
1 hour post prandial BG	110 – 140 mg/dL
2 hour post prandial BG	100 – 120 mg/dL
CGM Users	
Time in range (70-180)	> 70%
Time below range (<70)	< 4%

ADA. Standards of Care. 2024.

Gestational Diabetes Management

Stop harmful medications prior to conception

- ACEi, ARBs, statins

Lifestyle adjustments are essential

- MNT, physical activity, weight management

Insulin preferred (basal or MDI)

- Metformin and glyburide not preferred as first line

Pre-eclampsia prevention

- ASA 81mg daily starting week 12-16
- BP management (nifedipine, labetalol)

Postpartum care

- Insulin resistance drastically changes immediately postpartum; close adjustments needed

ADA. Standards of Care. 2024.

Hospitalized Patients

- Check HbA1C on admission if no recent lab available
- Initiate therapy if BG ≥ 180 mg/dL persists
- Glycemic goal generally 140 – 180 mg/dL for non-ICU patients
- For patients using CGM, it should be continued during hospitalization
- For patients using AIDS, it should be continued during hospitalization
- POCT glucose checks can be used to confirm BG for insulin decision making

ADA. Standards Care. 2024.

Hospitalized Patients

Insulin is preferred treatment

- Basal or basal + bolus correction
- Discourage use of correction insulin only without basal insulin

Non insulin agents

- T2DM + HF: initiate/continue SGLT2i and upon discharge if not CI
- DPP4i may be safer/simpler with mild hyperglycemia on admission (BG < 180 – 200 mg/dL)
- GLP1-RA inpatient benefit unknown, but should be initiated in patients at discharge with compelling indications

ADA. Standards Care. 2024.

Things to come..

Once Weekly Basal Insulin

- Insulin icodec
- Insulin efsitora alfa

Incretin Drugs

- Dual and triple incretins
- More oral options
- Data on GLP1-RA in T1DM to reduce insulin use

Tirzepatide Trials

- SUMMIT: obesity + HFpEF
- SURPASS-CVOT: CV outcome vs. dulaglutide
- TREASURE-CKD: obesity + CKD

CONCLUSIONS

Summary

- Emphasize the use of DSMES, MNT, and physical activity in ALL patients with diabetes
- Recommend the use of technology to ease the management of diabetes
- Consider cardiorenal risk factors when determining treatment of diabetes

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